Andrographis paniculata in the treatment of upper respiratory tract infections: a systematic review of safety and efficacy

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CRD summary
This review evaluated a herbal medication for symptoms of upper respiratory tract infection. The authors concluded that Andrographis paniculata may be an effective treatment with few adverse effects and that further research is justified. The conclusions are in line with the evidence presented and appear appropriately cautious.

Authors' objectives
To assess the efficacy and safety of Andrographis paniculata (A. paniculata) in the treatment of upper respiratory tract infection (URTI).

Searching
MEDLINE, EMBASE, CINAHL, AMED, the Cochrane Library and the British Library's Index of Conference Proceedings were searched, all from inception to June 2003. The search terms were reported and no language restrictions were imposed. The authors also searched the reference lists of retrieved papers and departmental files. Manufacturers and distributors of A. paniculata products were contacted for relevant published or unpublished material. Data on adverse event reports were requested from the World Health Organization (WHO) and the drug safety bodies of the UK, Australia and Germany.

Study selection
Study designs of evaluations included in the review
Double-blind controlled trials were eligible for inclusion in the efficacy review; two of the included studies were not randomised. All types of study design were eligible for inclusion in the safety review.

Specific interventions included in the review
Studies of single or combined preparations of oral A. paniculata were eligible for inclusion. The studies included in the efficacy review used standardised extracts of A. paniculata alone or in combination with Eleutherococcus senticosus, except for one study that used a crude drug preparation. The comparator interventions for efficacy studies were placebo or paracetamol. The daily dose of andrographolide ranged from 48 to 360 mg/day in the efficacy review and from 11 mg/day to 10 mg/kg per day for studies included in the safety review.

Participants included in the review
Studies of patients with uncomplicated URTI were eligible for inclusion in the efficacy review. There were no restrictions on participants for the review of safety, and participants in the included studies were healthy volunteers, human immunodeficiency virus (HIV)-positive people, patients with renal stones and patients with cardiac and cerebrovascular disease, as well as those with URTI.

Outcomes assessed in the review
No inclusion criteria for the outcomes were specified. The outcomes assessed in the efficacy review were symptoms and days of sick leave. The outcomes in the safety review were all adverse events experienced.

How were decisions on the relevance of primary studies made?
One reviewer selected studies and a second reviewer checked the selection. Any disagreements were resolved by discussion.

Assessment of study quality
Validity was assessed using the Jadad scoring system, which gives a quality score (0 to 5) based on methods of randomisation and blinding and the description of withdrawals and drop-outs. One reviewer assessed the validity of the studies and a second reviewer checked the assessment. Any disagreements were resolved by discussion.

Data extraction
One reviewer extracted the data and a second reviewer checked the extraction. Any disagreements were resolved by discussion. Study details were extracted according to predefined criteria.

Methods of synthesis
How were the studies combined?
The results for efficacy and safety were tabulated and discussed in the text. The possibility of publication bias was discussed in the text.

How were differences between studies investigated?
Differences between the studies were presented in the text and tables.

Results of the review
Seven controlled trials (n=896) were included in the efficacy review. Fourteen studies (n=1,235) were included in the review of safety.

Efficacy.
The included trials scored between 3 and 5 for methodological quality. Significant differences in outcomes suggested that A. paniculata is superior to placebo in alleviating subjective symptoms of URTI.

Safety.
One study in HIV-positive patients and healthy volunteers, which used a high dose of andrographolide, was terminated early because of a large number of adverse events. Adverse events in the remaining trials were described as mild, infrequent and reversible. The WHO and drug manufacturers provided details of three and five adverse reaction reports, respectively.

Authors' conclusions
A. paniculata may be an efficacious treatment for the symptoms of uncomplicated URTI. Further research is warranted. Short-term treatment at recommended doses is associated with few reports of adverse events.

CRD commentary
The review question and the inclusion criteria were clear, except that inclusion criteria for the outcomes were not specified. The authors searched a wide range of appropriate sources without language restrictions and attempted to locate unpublished material. Validity was assessed for the efficacy review, although the method used (Jadad scale) was not the most informative. The study selection, validity assessment and data extraction stages were not performed independently, but checks performed by a second reviewer provided some protection against bias and errors during the review process.

Some relevant details of the included studies were presented in the text and tables. The authors' decision not to combine the efficacy results by meta-analysis seemed appropriate. The limitations of the available evidence, particularly with regard to safety, were addressed in the discussion and the possibility of publication bias was also noted. The authors' conclusions are in line with the evidence presented and appear appropriately cautious.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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